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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/676,707	09/30/2003	May Tom-Moy	10031347-1	8124

7590 07/21/2005

AGILENT TECHNOLOGIES, INC.
Legal Department, DL429
Intellectual Property Administration
P.O. Box 7599
Loveland, CO 80537-0599

EXAMINER	
LUM, LEON YUN BON	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 07/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/676,707	TOM-MOY ET AL.	
	Examiner	Art Unit	
	Leon Y. Lum	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

9-0-0

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-7 and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. In claim 1, line 8, the term "enhancement reaction" is vague and indefinite. The specification does not provide a clear definition for the term and one of ordinary skill in the art at the time of the invention would not know what type of reaction is being claimed.

4. Claim 7 is vague and indefinite because it is not clear how the term "plurality of targets" further limits the parent claim (claim 1). The parent claim recites the phrase "detecting a target" (line 1), which indicates that only one target is detected. Since the instant claim refers to a plurality targets, it is not clear how a plurality of targets further limits a single target.

5. In claim 11, the term "integrated storage means" is vague and indefinite. The specification does not provide a definition for the term and it is unclear whether the term refers to an electronic storage element, a physical storage element, a chemical storage element, or another type of storage element.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 8-11 and 13-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Eggers et al (US 5,670,322).

Eggers et al reference teaches an array of test sites 14 (i.e. plurality of features), each test site comprising a well 20 in an insulating layer 22 (i.e. pad or resistive material) with first and second plates 24a-b formed on two sides of the well to serve as a localized electrode pair, a probe 26 attached to the bottom of the well (i.e. probe disposed between first and second electrode), and detection circuitry 16 on-chip that addresses each test site (i.e. integrated addressing circuitry allows interrogation of features). See column 3, line 63 to column 4, line 53; and Figures 1 and 2a-b.

With regards to claim 10, Eggers et al teach recognition circuitry 18 (i.e. measurement circuitry) connected to the detection circuitry 16. See column 3, lines 63-66 and Figure 1.

With regards to claim 11, Eggers et al teach that other circuitry for processing information may be provided (i.e. integrated storage means). See column 4, lines 31-33.

With regards to claims 13-14, Eggers et al teach that different probes are used in test sites 14 for simultaneous detection of a plurality of different targets (i.e. each of plurality of different features comprises a different probe), wherein the probes are oligonucleotides (i.e. polynucleotides). See column 4, lines 7-11.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.

3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1-5 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Park et al (Science, 2002) in light of Fluke Corporation (Fluke Model 187 & 189 True RMS Multimeter Users Manual, 2000), and in view of Eggers et al (US 5,891,630).

Park et al reference teaches the electrical detection of DNA by detecting binding between a capture oligonucleotide strand located in the gap between two fixed microelectrodes and a longer target oligonucleotide in solution (i.e. contacting feature with sample; probe disposed between first and second electrode; polynucleotide). See page 1503, middle column, 2nd paragraph to right column, 1st paragraph. Park et al also teach an array of 4 electrode pairs with a different oligonucleotide capture strand in the electrode gap (i.e. microarray with a plurality of features; plurality of targets are detected). See page 1503, right column, 3rd paragraph to page 1504, left column, 1st

paragraph. In addition, Park et al teach the step of increasing the sensitivity of the device by exposing the active component of the device to a solution of Ag(I) and hydroquinone (i.e. applying an enhancement reaction to feature). See page 1503, right column, 2nd paragraph. Park et al further teach capacitance or conductivity measurements to determine the number of target molecules that fill the gap (i.e. analyzing the results to detect the target). See page 1503, right column, 2nd paragraph. Furthermore, Park et al teach measuring the resistance value across the gaps with a Fluke 189 multimeter (i.e. select one of the plurality of features to be interrogated; measuring the observable property at the selected feature). See page 1504, left column, 3rd paragraph to middle column, 1st paragraph. Since the Fluke 189 multimeter can only perform one measurement at a time, the detection of the 4-electrode pair array necessarily requires sequential detection, which indicates that the electrode pairs are selectively interrogated (i.e. repeating steps (c) and (d) to selectively interrogate each of the plurality of features). See Fluke Corporation, pages 2-4, 2-17, 3-6, and 3-7.

However, Park et al fail to teach that the substrate comprises integrated addressing circuitry in operable relation to each of the plurality of features and also fail to teach the step of providing a signal to the addressing circuitry to select one of the plurality of features to be interrogated.

Eggers et al reference teaches detection circuitry 16 on-chip, wherein a varying signal of frequency can be applied to each site, in order to enable fast detection of hybridization for large DNA probe arrays. See column 4, lines 16-18; column 7, lines 30-32 and lines 44-46; and Figure 1.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method and apparatus of Park et al with detection circuitry 16 on-chip, as taught by Eggers et al, in order to enable fast detection of hybridization for large DNA probe arrays. The detection circuitry of Eggers et al therefore provides an advantage over the multimeter of Park et al since the detection circuitry is able to interrogate a large number of electrode pairs in a short amount of time, whereas the handheld multimeter of Park et al would require a large amount of time to test each electrode pair in a large array. In addition, one of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including the detection circuitry of Eggers et al, in the apparatus of Park et al, since Park et al teach dual electrodes to detect hybridization in an array, and the detection circuitry of Eggers et al is connected to a plurality of electrode pairs that also detect hybridization.

With regards to claims 3-5, Park et al teach that the target oligonucleotide is attached to Au nanoparticles at one end (i.e. gold nanoparticle label) and that Ag(I) and hydroquinone is added after the binding of target and capture oligonucleotides (i.e. attaching a label to target prior to applying the enhancement reaction; deposits metal). See page 1503, right column, 1st paragraph; and Figure 1 and caption.

5. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Park et al (Science, 2002) in light of Fluke Corporation (Fluke Model 187 & 189 True RMS Multimeter Users Manual, 2000), and in view of Eggers et al (US 5,891,630) as applied to claims 1, 3, and 6 above, and further in view of Cheung (US 5,132,242).

Park et al and Eggers et al references have been disclosed above, but fail to teach that the label is attached to the target via a biotin-avidin conjugate binding pair.

Cheung reference teaches conjugation of DNA to microspheres using avidin and biotin, in order to take advantage of the strong non-covalent interaction between avidin and biotin. See column 10, lines 46-53.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Park et al and Eggers et al with conjugation of DNA to microspheres using avidin and biotin, as taught by Cheung, in order to take advantage of the strong non-covalent interaction between avidin and biotin. The avidin-biotin conjugation to connect DNA to microspheres, as taught by Cheung, provides an advantage over the oligonucleotide-modified particles of Park et al and Eggers et al, since the avidin-biotin conjugation provides a strong interaction that would not allow dissociation of the microspheres from the bound targets and result in false negatives. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including the avidin and biotin binding pairs, as taught by Cheung, in the method of Park et al and Eggers et al, since Park et al and Eggers et al teach particles bound to nucleic acids, and the avidin and biotin binding pairs of Cheung are able to conjugate microspheres, a type of particle, to nucleic acids.

6. Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Eggers et al (US 5,891,630) in view of Mallet et al (US 6,660,533 B2).

Eggers et al reference has been disclosed above, but fails to teach that the pad of resistive material is metal oxide.

Mallet et al reference teaches metal oxides surfaces, in order to provide an immobilization that is engenders very good signal to background noise ratios, and stable immobilization. See column 2, lines 45-53.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the apparatus of Eggers et al with metal oxides surfaces, as taught by Mallet et al, in order to provide an immobilization that is engenders very good signal to background noise ratios, and stable immobilization. By providing good signal to background noise ratios, the binding of Eggers et al would be more accurately detected. In addition, one of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including the metal oxide surfaces of Mallet et al, in the apparatus of Eggers et al, since Eggers et al teach biomolecule immobilization onto surfaces, and the metal oxide of Mallet et al is one type of surface that can immobilize biomolecules.

7. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Eggers et al (US 5,891,630) in view of Sandstrom (US 6,545,758 B1).

Eggers et al reference has been disclosed above, but fails to teach at least one reference feature in operable relation to the addressing circuitry.

Sandstrom reference teaches control sites on a microarray, in order to compare experimental probe sites to a reference or purposefully mismatched site for eliminating

signal from background signal and nonspecific hybridization. See column 4, line 61 to column 5, line 17.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the apparatus of Eggers et al with control sites on a microarray, as taught by Sandstrom, in order to compare experimental probe sites to a reference or purposefully mismatched site for eliminating signal from background signal and nonspecific hybridization. The control sites of Sandstrom therefore provide the advantage of determining accurate detection in the binding sites of Eggers et al. In addition, one of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including control sites, as taught by Sandstrom, in the apparatus of Eggers et al, since Eggers et al teach an array of binding sites, and the control sites of Sandstrom can also be placed in an array of binding sites.

Double Patenting

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 1-15 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-31 of copending Application No. 10/676,957 in view of Park et al (Science, 2002) and Eggers et al (US 5,891,630).

Claims 1-15 of the instant application recite an apparatus and method of contacting a microarray with a sample, the microarray comprising a plurality of features disposed on a substrate, each feature comprising a probe in between a first and second electrode disposed on the substrate, the substrate comprising integrated addressing circuitry in operable relation to each of the plurality of features, applying an enhancement reaction to the plurality of features to result in a change in an observable property of at least one of the plurality of features, providing a signal to the addressing circuitry to select one of the plurality of features to be interrogated, measuring the observable property at the selected feature, repeating steps (c) and (d) to selectively interrogate each of the plurality of features, and analyzing the results obtained from step (d) to detect the target.

Claims 1-31 of the copending application teach an apparatus and method of contacting an array of devices with a sample, each device comprising a plurality of electrodes adjacent a pad of resistive material and approve supported on the pad of resistive material, applying an enhancement reaction to the results of (a) to result in a change in an observable property of each of a subset of the devices on the array of

devise, measuring the observable property at each of the subset of devices using at least one o said plurality of electrodes of each device of the subset, and evaluating the results of (c) to analyze the sample for the plurality of targets.

However, claims 1-31 of the copending application fail to teach that the probe is in between a first and second electrode, the substrate comprises integrated addressing circuitry, providing a signal to the addressing circuitry to select one of the plurality of features to be interrogated, measuring the observable property at the selected feature, and repeating steps (c) and (d) to selectively interrogate each of the plurality of features.

Park et al reference teaches a capture oligonucleotide strand located in the gap between two fixed microelectrodes for detecting a target oligonucleotide (i.e. probe in between a first and second electrode), wherein the detection is performed on a 4-electrode pair array using a multimeter (i.e. select one of the plurality of features to be interrogated; measuring the observable property; repeating steps (c) and (d) to interrogate each of the plurality of features), in order to perform DNA detection without requiring additional reagents that current systems require. See page 1503, left column, 1st paragraph; page 1504, left column, 3rd paragraph to middle column, 1st paragraph; and Figure 1 and caption.

Eggers et al reference teaches detection circuitry 16 on-chip, wherein a varying signal of frequency can be applied to each site, in order to enable fast detection of hybridization for large DNA probe arrays. See column 4, lines 16-18; column 7, lines 30-32 and lines 44-46; and Figure 1.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method and apparatus of claims 1-31 of the copending application with a capture oligonucleotide strand located in the gap between two fixed microelectrodes for detecting a target oligonucleotide (i.e. probe in between a first and second electrode), wherein the detection is performed on a 4-electrode pair array using a multimeter (i.e. select one of the plurality of features to be interrogated; measuring the observable property; repeating steps (c) and (d) to interrogate each of the plurality of features), as taught by Park et al, in order to perform DNA detection without requiring additional reagents that current systems require, and with detection circuitry 16 on-chip, wherein a varying signal of frequency can be applied to each site, as taught by Eggers et al, in order to enable fast detection of hybridization for large DNA probe arrays. The dual electrodes of Park et al and the detection circuitry of Eggers et al therefore provide the advantages of simpler and faster detection, respectively, of the binding of the copending application. One of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including the dual electrodes of Park et al and the detection circuitry of Eggers et al, in the copending application, since the copending application teach arrays, and the electrodes and circuitry of Park et al and Eggers et al, respectively, are applicable to arrays.

This is a provisional obviousness-type double patenting rejection.

Conclusion

10. No claims are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leon Y. Lum whose telephone number is (571) 272-2878. The examiner can normally be reached on weekdays from 8:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Leon Y. Lum
Patent Examiner
Art Unit 1641

LYL

Christopher L. Chin

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641
7/18/05